UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,081	11/13/2003	Nathan Ravi	111828-00110	7277

27557 7590 12/12/2007

BLANK ROME LLP
600 NEW HAMPSHIRE AVENUE, N.W.
WASHINGTON, DC 20037

EXAMINER	
ROBERTS, LEZAH	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/706,081	RAVI, NATHAN	
	Examiner	Art Unit	
	Lezah W. Roberts	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-121* is/are pending in the application.

4a) Of the above claim(s) *1-22, 30, 32, 33, 46-116 and 121* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-29,31,34-45,117 and 118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *13 May 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election of Species and Restriction Requirement

Applicant's election with traverse of Group II in the reply filed on May 7, 2007 and the species of hydroxyethylmethacrylate as the monomer/copolymer, DTT for the reducing agent, N,N'-bis(acryloyl)cystamine as the crosslinker, atomospheric oxygen as the oxidizing agent, hydrophilic as the hydrogel and polymers as the particle in the reply filed September 25, 2007 is acknowledged. The traversal is on the ground(s) that all groups and species are related in some manner to hydrogel formation and therefore there is not a substantial burden of an additional search in order to examine all the claims of the invention. This is not found persuasive because the claims recite compositions which may be used in other areas other than the eye. The claims also recite different methods that although recite hydrogels are distinct from one another.

The requirement is still deemed proper and is therefore made FINAL.

Claims

Claim Rejections - 35 USC § 102 - Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section

351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1) Claims 23, 25, 44, 45, 117 and 118 are rejected under 35 U.S.C. 102(e) as being anticipated by Sawhney (US 6,818,018).

Sawhney discloses *in situ* polymerizable hydrogels for use in the eye. The hydrogels are formed by a combination of physical and chemical crosslinking processes where the physical crosslinking is mediated by one or more natural or synthetic components that stabilize the hydrogel-forming precursor solutions at a deposition site for a period of time sufficient for more resilient chemical crosslinks to form. Methods of using the tissue coatings include preventing postsurgical adhesion formation, as tissue augmentation or luminal occlusion aids, as matrices for carrying cells, drugs or other bioactive species, as tissue sealants or adhesives, and as medical device coatings (see Abstract). The hydrogel may be permanent or bioabsorbable. When bioabsorbable at least one linkage is susceptible to cleavage ether by hydrolysis, by thermal degradation or by other physiological processes. Physical crosslinking is mediated by one or more natural or synthetic components that act individually or synergistically to stabilize the hydrogel-forming precursor solution at a deposition site for a period of time sufficient for more resilient chemical crosslinks to form. The physical crosslinks are reversible, this encompasses the instant claims. Monomers suitable for chemical crosslinking include hydroxyethyl methyacrylate and acrylamide (col. 10, lines 30-67). It may be concluded that the chemical crosslinked compositions are reversible to an extent because they may be bioabsorbable and at least one bond is susceptible to cleavage. The

compositions may be used to protect the eye and hug the eye like a contact lens (col. 23, lines 55-67), encompassing claims 44 and 45. The compositions may comprise release rate modification agents such as polyethylene glycol, which is a polymer encompassing claim 118 (col. 18, line 34). In regards to the pH, physiological pH is about 7, encompassing claim 29. In regards to the oxidizing agent, the gel is made when the compostions are mixed which is in the presence of oxygen encompassing claim 39. The reference anticipates the instant claims insofar as it discloses a method for forming a hydrogel *in situ* in an eye comprising introducing a reversible hydrogel system in solution into the eye and gelling the reversible system by oxidation.

2) Claims 23-26, 29, 31, 34-36, 38-42, 44 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Hodd et al. (US 6,861,065).

Hodd et al. disclose a method of producing intraocular lenses *in vivo*. Solutions comprising monomers and photoinitiators are administered to the capsular bag of the eye, wherein light initiates a reaction between the monomers and initiators forming a gel (col. 3). The monomers used include N-vinyl-pyrrolidone and acrylamide such as dimethyl acrylamide. Crosslinking agents added to the compositions include functional groups such as hydroxyethylmethacrylate. Other crosslinking agents include azo-isobutyronitrile (col. 6 and see Examples). In regards to the term hydrogel and the systems being reversible, it may be concluded that because the compositions are substantially the same as those recited in the instant claims, comprising N-vinyl-pyrrolidone, acrylamide and crosslinking agents hydroxyethylmethacrylate and azo-

isobutyronitrile in solution, that when a gel forms in the capsular bag, it forms a hydrogel that is reversible to a solution under the appropriate conditions. The reference anticipates the instant claims insofar as it discloses a method for forming a hydrogel *in situ* in an eye comprising introducing a reversible hydrogel system in solution into the eye and gelling the reversible system with light.

Claim Rejections - 35 USC § 103 - Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) Claims 23-29, 31, 34-39, 44, 45 and 117-118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marchant (US 2002/0068087) in view of Viegas et al. (US 2003/0143274).

Marchant discloses hydrogels which is bioadhesive composition comprising two or more essentially excretable, essentially non-degradable polymer backbones. The

polymer backbones are crosslinked, and said crosslink is degradable in a mammal. The hydrogel demonstrates bioadhesion to a mucosal surface that is crosslinked by a degradable linkage such as disulfide for use inside the body (see Abstract). The compositions act as drug carriers and deliver the drug to areas such as the eyes. The hydrogels are susceptible to reduction and oxidation. The polymer backbone comprises subunits selected from the group consisting of polyacrylic acids, polymethacrylic acids, allyl, allyl amines, acrylic acid esters, amides, pH-sensitive monomers, N-vinyl pyrrolidones, hydroxyethylmethacrylates (HEMA), and combinations thereof (paragraph 0044). Crosslinkers include bis N,N'-acrylamide cystamine. Any thiol containing reagents such as dithiothreitol, dithioerythritol, 2 mercaptoethanol and mercaptoethylamine, and cysteine can serve as reducing agents for disulfides (paragraph 0072). The reference differs from the instant claims insofar as it does not disclose the hydrogels are formed *in situ*.

Viegas et al. disclose medical uses of *in situ* formed gels. The gels may be used to deliver medicaments to the eye. The compositions are useful, with or without the inclusion of a medicament, as injectable compositions for depot drug delivery, as a protective corneal shield, as a second skin for application to wounds, as an ablatable corneal mask in a laser keratectomy process, or as medical devices. The films made by the compositions are characterized as thin, soft hydrophilic corneal contact lenses (paragraph 0080). Polymers of methylmethacrylate and 2-hydroxyethyl methacrylate may be used in the compositions. The compositions of the invention are low viscosity liquids at ambient temperatures; they easily pass to various ophthalmic areas insuring

maximum contact between exposed tissue and the composition of the invention, which form gels at the point of treatment (paragraph 0023). The gel compositions of the invention can be either peeled away or allowed to be absorbed over time. If an irreversible gel is required or an elastic gel, that is, one that retains its shape, cross-linking is required. Cross-linking is the physical, covalent or ionic bonding of two or more molecules of the same polymer (paragraph 0042). The reference differs from the instant claim insofar as it does not disclose the type of crosslinking agent or that the compositions are reversible although it does disclose the compositions may be absorbed over time.

It would have been obvious to one of ordinary skill in the art to have administered the components of the compositions in the primary reference as a liquid to the eye to form a hydrogel *in situ* motivated by the desire to ensure that the compositions easily passed to various ophthalmic areas insuring maximum contact between exposed tissue and the compositions, as disclosed by the secondary reference.

Alternatively it would have been obvious to use the crosslinking agents and methacrylate monomers in the method of treating the eyes in the secondary reference motivated by the desire to use components that are cleared from the systems when the compositions are absorbed by the body, as disclosed by the primary reference.

2) Claims 24, 26-29, 31 and 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney (US 6,818,018) in view of Marchant (US 2002/0068087).

Sawhney is discussed above. The reference differs from the instant claims insofar as it does not disclose N,N'-bis(acryloyl)cystamine as a disulfide crosslinker.

Marchant is discussed above. The reference differs from the instant claims insofar as it does not disclose the compositions are applied to an eye *in situ*.

It would have been obvious to use the crosslinking agents and methacrylate monomers in the methods of treating the eyes in the primary reference motivated by the desire to use components that are cleared from the system when the compositions are absorbed by the body, as disclosed by the secondary reference.

Claims 23-29, 31, 34-45, 117 and 118 are rejected.

Claims 1-22, 30, 32, 33, 46-116 and 121 are withdrawn.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lezah Roberts
Patent Examiner
Art Unit 1614

Frederick Krass
Primary Examiner
Art Unit 1614